REMARKS

Claims 1-22 and 75-94 are pending in the instant application.

Process claims 23-44 were previously withdrawn from consideration, Applicants reserve the right to rejoin the withdrawn process claims upon the allowance of one or more of the product claims from which they depend (MPEP §821.04).

Claims 1, 23, 28, and 34 are hereby amended. Support for the amended claims can be found throughout the application as originally filed. Claim 22 is hereby canceled without prejudice or disclaimer in the interest of expediting the allowance of the application.

Applicants acknowledge the Examiner's withdrawal of the following rejections:

(i) rejection of claims 1-22 and 75-93 under §102(a) and §102(e) in view of Lois-Cabelle et al. (US 2003/0059944A1); and

(ii) rejection of claims 1-3, 7-19, 22, 75, 76, 79, 90, and 83-94 under §102(e) in view of Engelke et al. (US 2003/0148519A1);

With respect to the remaining rejections, Applicants respectfully request reconsideration and examination of this application and the timely allowance of the pending claims in view of the arguments presented below.

I. Claim Rejections -35 USC §112

The Examiner has maintained the rejection of claim 22 under 35 USC §112, first paragraph, for allegedly failing to comply with the written description requirement. Without acquiescing to the rejection and solely in the interest of expediting the allowance of the application, Applicants have canceled claim 22, thereby rendering the rejection moot.

II. Claim Rejections -35 USC §102

a. Rejection of Claims 1-3, 8-11, 14-19, 22, 77-81, 84 and 86-94 under 35 U.S.C. § 102(a) in view of Park et al.

The Examiner has newly rejected claims 1-3, 8-11, 14-19, 22, 77-81, 84 and 86-94 under 35 U.S.C. § 102(a) as allegedly being anticipated by Park *et al.* (Nucleic Acids Research Supplement (2001), No. 1, pp. 219-20). Although the Examiner appears to recognize that the

dsRNAs of Park et al. are ***long dsRNAs***, the Examiner nevertheless alleges that Park et al. "inherently taught" siRNAs on the grounds that the ***long dsRNAs*** of Park et al. would be processed in cells to produce siRNAs.

Applicants traverse the rejection with respect to the amended claims.

Applicants submit that issue of whether or not the ***long dsRNAs*** of Park et al. are inherently processed in cells is not relevant to the claimed invention. Applicants have amended the claims to more clearly specify that the siRNA molecules of the invention are ***isolated*** siRNA molecules. An isolated siRNA is one which is produced synthetically, recombinantly, or enzymatically but which is separated from the components with which it normally exists in nature. Thus, even if the ***long dsRNAs*** of Park et al. produced siRNA within a cell they would not be ***isolated*** siRNA. Since Park et al. does not anticipate the claimed invention, either explicitly or inherently, Applicants respectfully request withdrawal the rejection.

b. Rejection of Claims 1-3, 8-11, 14-22, 77-81, 84 and 86-94 under 35 U.S.C. § 102(e) in view of McSwiggen et al.

The Examiner has maintained the rejection of claims 1-3, 8-11, 14-22, 77-81, 84 and 86-94 under 35 U.S.C. § 102(e) in view of McSwiggen et al. (US 2003/0175950A1). In particular, the Examiner alleges that a McSwiggen et al. priority document (US Provisional Patent Application No. 60/374,722, filed April 23, 2002) provides support at pages 3, 9-11, 22, 23, 43, 52-54, and 107-110 for the embodiments relied upon in the rejection. Applicants traverse the rejection.

Applicants submit herewith a Declaration under 37 C.F.R. §1.131 (herein, "Declaration") by Drs. Mario Stevenson and Jean-Marc Jacque, co-inventors of the instant application. It is the Applicant's position that the Declaration obviates the Examiner's rejection based on McSwiggen *et al.* As described in the Declaration (filed herewith), Applicants' invention was completed prior to the filing date (April 23, 2002) of the McSwiggen *et al.* priority document (60/374,722) relied upon by the Examiner. Applicants submit that the data referenced in the Declaration is also reproduced in the working examples set forth in the specifications of the instant application and its priority documents (US Provisional Applications 60/428,631 and 60/444,893). Accordingly, for at least these additional reasons, McSwiggen *et al.* is not available for use by the Examiner as a reference, either basic or auxiliary, in the rejection of the claims of the present

application under 35 U.S.C. §102(e). Therefore, it is clear that the above-quoted rejection of claims 1-3, 8-11, 14-22, 77-81, 84 and 86-94 under 35 U.S.C. § 102(e) in view of McSwiggen *et al.* should be reconsidered and withdrawn.

Applicants wish to reiterate that a §131 Declaration is properly admissible to remove McScwiggen *et al* as a prior art reference under 35 U.S.C. §102(e), since the currently pending claims of McSwiggen *et al.*[1], ***are not directed to the same patentable invention*** claimed by Applicants. Should the Examiner consider the claims to conflict, Applicants respectfully submit that the Declaration should be nevertheless be entered and considered as provided by MPEP 2305 (I), which states:

> "Similarly, if a published application contains claims to the same invention, but the claims in the published application are not in condition for allowance, then no interference is yet possible. 37 CFR 41.102. Since the claims in the published application might never be allowed in their present form, it is not appropriate to proceed as though an interference might be inevitable. Consequently, an affidavit under 37 CFR 1.131 may be submitted."

Accordingly, since the pending claims of McSwiggen *et al.* are not in condition for allowance[2], Applicants submit that the Declaration should be entered and the reference removed from consideration.

III. Claim Rejections -35 USC §103

The Examiner has newly rejected claims 1-11, 14-22, 77-84 and 86-94 under 35 U.S.C. § 103(a) for alleged obviousness over Draper et al. (US Patent No. 5,693,535; filed August 13, 1997; granted October 26, 1999) in view of Tuschl et al. (US Patent No. 7,056,704; filed April 27, 2004; granted June 6, 2006). Specifically, the Examiner alleges that "it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the siRNAs of Tuschl for the ribozymes of Draper when targeting HIV for degradation" (see page 8 of Office Action). The Examiner states that "one would have had a reasonable expectation of success because the target sites of Draper were selected on the basis of their availability for hybridization". Applicants respectfully disagree.

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[1] The Examiner is directed to the claim amendments filed in US Application 10/225,023 on August 16, 2007.
[2] The Examiner is directed to the Final Rejection mailed on November 1, 2007.

As an initial matter, Applicants submit that the skilled artisan at the time of the invention would not have be motivated to turn to ribozyme art in order to arrive at the claimed invention. As the Examiner is aware, siRNAs (unlike the ribozymes of Draper et al.) are not self-catalytic RNA molecules. Rather, siRNAs must form a RNA-induced silencing complex (RISC) with one or more protein subunits in order to have endonuclease activity. Moreover, siRNAs are structurally distinct from ribozymes which have complex secondary structure. Since siRNAs and ribozymes are structurally and functionally distinct from each other, one skilled in the art would not rely on the teachings of Draper et al., as Draper et al. is non-analogous art.

Even if one skilled in the art were to rely on the cited references, the prior art objectively demonstrates that the skilled artisan would have had no reasonable expectation of success in applying siRNA technology to mediate RNA interference (RNAi) of the viral RNA genome of an RNA virus such as HIV. At the time of Applicant's invention it was thought that the ***genomic RNA*** of RNA viruses would not be amenable to siRNA degradation. For example, Bitko et al. found that the genomic viral RNA of Respiratory Syncitial Virus (RSV) was resistant to degradation by complementary siRNAs and suggested that ***viral genomic RNA***, as it exists encapsidated within a nucleocapsid complex, is inaccessible to the RNAi silencing complex (see pg. 8, first full paragraph of Bitko V. & Barik S., *BMC Microbiol.*, 1:34-45 (2001); reference C5 in IDS submitted 7/16/07). In contrast, Applicants made the surprising and unexpected discovery that the genomic RNA of HIV (an RNA virus) is fully susceptible to siRNA. Moreover, the publication of Applicants' invention in a highly prestigious scientific journal (*Nature*) supports the non-obviousness of the invention (see Exhibit A submitted herewith). Accordingly, Applicants respectfully submit that the rejection should be reconsidered and withdrawn.

CONCLUSION

In view of the above amendment and response, Applicants believe the pending application is in condition for allowance. Nevertheless, if a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By _____
Debra J. Milasincic
Registration No.: 46,931
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant